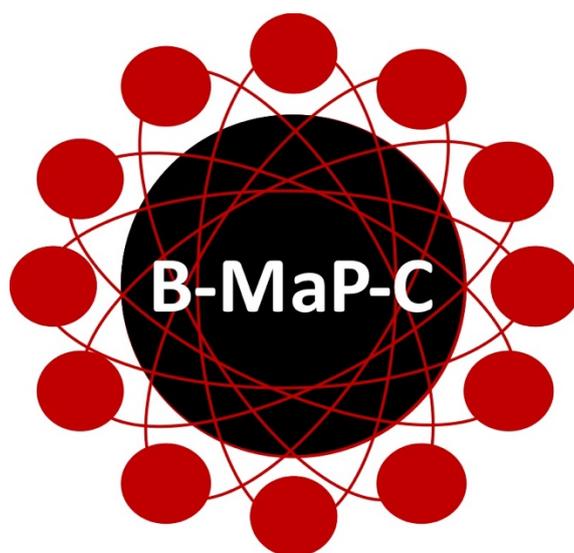


The **B-MaP-C** study

Breast Cancer **M**anagement **P**athways during
the **COVID-19** pandemic - a national audit

Study Protocol Version 14
11th May 2020



ABS
ASSOCIATION OF
BREAST SURGERY

Study Contact: COVID19breast@gmail.com

Study Website: bmapc.com

Audit Steering Committee

Rajiv V Dave - Lead Investigator and RedCap lead

Cliona Kirwan

Ashu Gandhi

Baek Kim

Ramsey Cutress

Audit Advisory Group

Kieran Horgan

Stuart Macintosh

Daniel Leff

Raghavan Vidya

Shelly Potter

Chris Holcombe

Chris Cartlidge

Rachel O'Connell (MFAC representative)

Tim Rattay (MFAC representative)

Alona Courtney (Trainee representative and IT lead)

Ellen Copson (Medical Oncology)

Charlotte Coles (Clinical Oncology)

Nisha Sharma (Radiology)

Patricia Fairbrother (Patient representative)

Please see Section 9 for roles and responsibilities of the Audit Steering Committee and the Audit Advisory Group

Background

1.1 COVID-19

With an epicentre in the Hubei Province of the People's Republic of China, the current outbreak of the novel coronavirus SARS-CoV-2 (coronavirus disease 2019, COVID-19), has spread world-wide. In January 2020, the WHO Emergency Committee declared a global health emergency (1). By the 31st of March, 2020, there were 788,522 cases confirmed worldwide, with 37,878 deaths (2). COVID-19 has led to worldwide repercussions in healthcare delivery, including that of cancer care (3).

1.2 Statements from professional bodies

1.2.1 Association of Breast Surgery

The Association of Breast Surgery published a guidance statement on 15th March 2020 in response to the ongoing threat of COVID-19 and the likely changes required to the management of patients presenting with breast symptoms and those with confirmed breast cancer. This included triage of all referrals to breast clinic, and precautionary advice to those patients with a high index of suspicion of breast cancer, who should continue to attend. There have been reports of suspension of all follow-up clinics and high risk surveillance nationally, and there is suspension of breast screening. A new model of telephone clinics has been employed.

Management of patients confirmed to have breast cancer may involve an adjusted treatment pathway (referred to as "COVID-altered" in this protocol). In the event of an anticipated shortage of theatre space, there will be prioritisation of patients being offered surgery. This will likely lead to more widespread use of primary and neoadjuvant endocrine therapy, and reduced use of neoadjuvant chemotherapy, which will likely be reserved for patients with inoperable disease, rather than for down-staging for breast and axillary conservation.

Specific guidance for patients diagnosed with breast cancer during the pandemic have been circulated to the ABS membership (4):

- Clip put in all cancers when biopsy performed.
- Aim for day case surgery in majority of patients.
- If theatre space is limited, surgical priority given to oestrogen receptor (ER) negative patients first, then HER2+ patients and then pre-menopausal ER+ patients.
- For ductal carcinoma in situ (DCIS) patients if theatre space available prioritise high grade DCIS.
- Neoadjuvant chemotherapy only for inoperable disease, NOT to downstage from mastectomy to BCS or to perform axillary conservation in ER- or human epidermal growth factor receptor 2 (HER2+) patients.
- No immediate breast reconstruction. Mastectomy and delayed reconstruction to be offered at a later date.
- If insufficient theatre capacity, post-menopausal ER+ patients to be commenced on primary endocrine therapy. If not enough theatre capacity premenopausal ER+ patients may also have to be commenced on primary endocrine therapy.
- Discuss with oncology whether all grade 3 or node positive ER+ positive patients should have genomic testing performed on the core biopsy. If a high score to have surgery as would normally need adjuvant chemotherapy. Currently genomic testing is not reimbursed in this situation, but this will need to be re-considered.

1.2.2 National Coordinating Committee for Breast Pathology (NCCBP)

The NCCBP have published specific guidance (5) to protect staff during preparation of large breast samples, for example by avoiding submission of fresh specimens being submitted to the laboratory and should instead be placed in formalin as soon as possible and all slicing should be carried out in a Microbiological Safety Cabinet. Guidelines have also been

developed for reporting of pathological specimens in the event that a specialist breast pathologist is unavailable.

1.2.3 Royal College of Radiology

International guidelines have been published on radiation therapy for breast cancer during the COVID-19 pandemic (6). In addition to this, the Royal College of Radiologists (RCR) have published national guidelines on the rationalisation of radiotherapy for breast cancer patients during the pandemic (7).

- Omit radiotherapy (RT) for patients 65 years and over (or younger with relevant co-morbidities) with invasive breast cancer that are up to 30 mm with clear margins, grade (G) 1-2, ER+, HER2- and node negative who are planned for treatment with endocrine therapy.
- Deliver RT in 5 fractions only for all patients requiring RT with node negative tumours that do not require a boost. Options include 28-30 Gy in once weekly fractions over 5 weeks or 26 Gy in 5 daily fractions over 1 week as per the FAST and FAST Forward trials respectively.
- Boost RT should be omitted to reduce fractions and/or complexity in the vast majority of patients unless they are 40 years old and under, or over 40 years with significant risk factors for relapse.
- Nodal RT can be omitted in post-menopausal women requiring whole breast RT following sentinel lymph node biopsy and primary surgery for T1, ER+, Her2, G1-2 tumours with 1-2 macrometastases.
- Consider delivering RT, 26 Gy in 5 fractions for patients requiring nodal radiotherapy who would have fulfilled the eligibility for the FAST Forward nodal subgroup study (not internal mammary chain (IMC) irradiation) and where nodal RT is still considered necessary during the COVID-19 pandemic.

Further guidelines have been published regarding the use of pre-operative breast radiotherapy in patients whose surgery is postponed (8).

- Newly diagnosed invasive breast cancer with no systemic therapy options (chemotherapy or endocrine) e.g. patient with ER- breast cancer but deemed unsuitable for chemotherapy as significantly increased risk of COVID-19 mortality.
- Completion of all neoadjuvant therapy with no option of endocrine and/or HER2 directed therapy e.g. patients with triple negative breast cancer.
- Loco-regional cancer progression/poor response despite use of all available neoadjuvant therapies including Her2 directed and/or endocrine therapy.

1.2.4 Cancer Core Europe

The 'Cancer Core Europe (CCE)' consortium have published a 'roadmap' for care of cancer patients during the COVID-19 pandemic (9). These are general consensus measures taken by CCE centres during the COVID-19 pandemic, which include re-structuring of service provision and amendments to usual protocols of radiation therapy and chemotherapy, with a clearly defined prioritisation scheme for anti-cancer therapy based on anticipated outcome. They offer opinion on critical research priorities, which includes to 'collect real-world data on the effects of adjustment and de-escalation of treatment regimens on the outcomes of patients with cancer.'

1.3 The impact of COVID-19 on working patterns and treatment pathways

The attendance at multi-disciplinary team (MDT) meeting will be minimal, in accordance with ABS guidelines, and it is likely that the primary treating clinician will not be present at the MDT. It is vital that the clinicians not present at MDT have an understanding of the altered

decision making process. Therefore, there is a need to contemporaneously capture standard and COVID-altered management decisions, not only to document the changes in treatment provision, but also to ensure that these decisions were deliberate, and not made in error (given increased pressures). This would ideally be performed prospectively, if only to develop an 'aspirational' dataset for further audit / interrogation. However, considering the pressures on the service currently, this can be done retrospectively.

1.4 Possible breast cancer management scenarios during the COVID-19 pandemic

1.4.1 Pre-operative setting

- Omitted/incomplete neoadjuvant chemotherapy, in particular for patients with HER2+ cancers and triple-negative cancers.
- No neoadjuvant chemotherapy for patients requiring down-staging to accommodate breast conserving surgery or axillary conservation
- Patients with hormone receptor positive cancers having primary/neoadjuvant endocrine therapy with a view to delayed surgery once the pandemic is under control.
- Patients having delayed surgery due to insufficient theatre capacity
- Changes to pre-op assessment, including altered imaging protocols and biopsy of 'incidental lesions'

1.4.2 Operative setting

- Patients having delayed (>31 days) surgery
- Patients having simple mastectomy, who have requested / would usually be offered immediate reconstruction, who are now having simple mastectomy
- Patients having mastectomy due to omission of RT, who would otherwise have been offered breast conserving surgery.

- Patients who are at high risk (>1:4 lifetime risk of developing breast cancer) who have developed unilateral breast cancer would otherwise be offered synchronous contralateral mastectomy but will be denied this option due to the strained service provision.
- Patients who would usually have margin re-excision surgery for close margins or completion axillary node clearance if significant nodal disease found at sentinel lymph node biopsy (based on local protocols), who do not have further surgery.

1.4.3 Post-operative setting

- Patients having breast conserving surgery who would usually have adjuvant RT to the breast +/- axilla, which has been omitted, potentially due to newly enforced protocols on patient selection
- Patients who would usually be offered adjuvant chemotherapy +/- targeted anti HER2 therapy, not having this, potentially due to a newly introduced significant increase in the threshold of chemotherapy benefit secondary to a concern of the consequences of chemotherapy immunosuppression during the COVID-19 pandemic
- Patients having genomic testing (e.g. ONCOTYPE), which has been used outside of NICE guidelines (2018) to direct adjuvant chemotherapy

1.5 Research collaboratives

There is a well-tested route for delivery of high-quality cohort/audit studies in the UK.

The first surgical trainee research collaborative was formed in the West Midlands, however, the collaborative network now has almost universal coverage of the UK (10). Specialty surgical trainee collaboratives have also emerged in neurosurgery, plastic surgery and are forming in other sub-specialties supported by the Royal College of Surgeons (11, 12).

These collaborations have the capacity to generate meaningful large scale data with the

potential to inform or change clinical practice (13-15). There have been several successful breast surgery related trainee collaborative studies, such as ibra (16) , ibra-2 (17), and TeaM (18) and other national non-trainee collaborations, including the Sloane project (19) and National Audit of breast cancer in older patients (NABCOP)(20).

2. Aims and objectives

The primary aim of the B-MaP-C national audit is:

- To document and describe breast cancer management (surgery, neoadjuvant / adjuvant chemotherapy and radiotherapy) during the COVID-19 pandemic and compare this to current (pre-COVID-19) management practice.

The secondary aims include auditing:

Short term:

- The proportion of patients on 'bridging' neoadjuvant endocrine therapy who progress or fail to respond and so require surgery for clinical reasons earlier than anticipated.
- The proportion of patients planned for breast conserving surgery, having completion mastectomy for oncological reasons due to altered indications for radiotherapy.
- The proportion of delayed reconstruction in patients who in a patient who would have been offered immediate reconstruction (and having simple mastectomies instead).
- Proportion of presumed DCIS found to have an invasive component at surgery (usually ~20%)

Long term:

- To gather a national cohort of patients with COVID-altered treatment pathways that can be interrogated in the future for oncological outcomes, including but not limited to:
 - Risk of increased loco-regional recurrence and/or poorer overall survival in patients having breast conserving surgery, and omitted radiotherapy.
 - Risk of increased loco-regional recurrence and/or poorer overall survival in patients having omitted neoadjuvant / adjuvant chemotherapy +/- targeted anti-HER2 therapy.
 - Risk of disease progression and/or poorer overall survival in premenopausal and postmenopausal patients on 'bridging' primary endocrine therapy having delayed surgery.

3. Definitions

Pre-COVID-19 management decision – This is the standard planned treatment, that the patient would have undergone in normal circumstances, prior to the COVID pandemic

COVID-19 management decision - This is the planned treatment as a result of the COVID-19 pandemic, which may be altered.

Primary Endocrine therapy – Patients not suitable for surgery due to co-morbidities, having primary endocrine therapy as their primary treatment.

Neo-adjuvant endocrine therapy – Patients having endocrine therapy for ‘bridging’ purposes, due to insufficient theatre space as a result of the COVID-19 pandemic, and are planned to have surgery at a later date

Incomplete or altered chemotherapy regimens – Full planned cycles/dose not given, to expedite surgery, or to mitigate against risk of COVID-19 whilst immunosuppressed.

Omitting some cycles of chemotherapy due to side effects or complications would not be included in this group unless it was a complication due to COVID-19.

Immediate reconstruction – Reconstruction at the time of mastectomy, which for purposes of this study includes temporary tissue expander.

4. Methods

This is a national collaborative project with an option to participate retrospectively or prospectively. Participation and data entry will be taken as approval for (anonymised) data to be used for publication purposes. It is recognised that workforce challenges may lead to logistic challenges and affect delivery of this study, in particular the redeployment of trainees away from the breast unit. As such, data collection will begin prospectively in volunteering units, based on availability of local resources and personnel.

4.1.1 Patient inclusion and exclusion criteria

Inclusion criteria

All patients with a new diagnosis of primary breast cancer (B5a, B5b, B5c) having treatment during the COVID-19 crisis. This includes patients discussed in the MDT from 16th March 2020 onwards, until normal services will resume, which will be determined locally, by availability of services and facilities.

This includes patients having either a 'standard' OR COVID-ALTERED plan (see flowchart on page 19). The inclusion of the standard patients is to allow for comparison and to achieve an idea of the 'denominator.'

Exclusion criteria

Patients with a new diagnosis of recurrent or metastatic breast cancer
All patients having surgery for benign breast disease
Patients having deferred surgery for symmetrising surgery and risk-reducing surgery
All patients with only B3/B4 lesions having surgery
All patients with established metastatic disease
All patients with established recurrent disease, with further recurrence
Incidental breast cancers detected on staging imaging for other non-breast cancers

4.1.2 Participation identification and recruitment

Participating centres will aim to recruit consecutive patients into the audit. Potential patients will be identified prospectively by the local participating clinical team via outpatient consultations, local MDTs, consultant surgeons and clinical nurse specialists. Prospective

data entry is recommended by guidance issued by professional bodies (see section 1) and would occur on a weekly basis, following the MDT meeting. It is accepted that in some cases retrospective ascertainment of patients will be necessary and that patient recruitment and data collection and entry will be completed according to local workforce availability

Simple demographic, procedure and process data will be contemporaneously collected for each participant. Data will be recorded in an anonymised format using a unique alphanumeric study identification number on a secure web-based database (REDCap) designed by Vanderbilt University(21-23) (<http://www.projectredcap.org/>).

It is vital that a secure record is kept locally of NHS numbers and corresponding RedCap ID. This will be necessary for a 'staged' data collection and future outcome studies.

To register for the study, participating units are requested to email COVID19breast@gmail.com to request access to the online database. Each unit will then be designated a unit ID (e.g. MFT), which will be used as a prefix for the patient ID (e.g. MFT001). It is of vital importance that a local secure record is kept of the RedCap ID with corresponding NHS numbers for future identification of patients. In the event of a trainee leading data collection, it is vital that this list is kept by the nominated consultant.

4.2 Case Record Form

Data field	Description
Section 1: Case record information	
RedCap record ID _____	This is your RedCap unit ID + patient number e.g. MFT001
Name of person entering data _____	
Name of consultant in charge of patient) _____	Please state as the consultant would be acknowledged in any publications
Patient Age at daignosis	
Date of cancer diagnosis.....dd/mm/yy	This is the date of diagnostic biopsy.
Date of first cancer surgery..... dd/mm/yy	If patient on 'bridging' neoadjuvant endocrine therapy, then leave blank for now, and return to fill out when surgery date available.
Where was Surgery performed? Red zone (operating theatre in acute care trust caring for COVID19 patients) / Green zone	

(operating theatre in cold site OR in private provider aiming to be COVID19 free site)	
Presentation: Symptomatic / Screen-detected	
Cancer T stage: 1/2/3 If bilateral or multifocal cancer, please enter data for the cancer for which an 'altered' pathway of management was recommended (bilateral), or the largest lesion (multifocal).	State the whole lesion size as per AJCC staging criteria. If pre-op (i.e. not having surgery or not yet had surgery), then this would be the largest size documented on MMG/USS/MRI. If post-op, then state pathological size.
Cancer N stage: 0/1/2	As per AJCC 8 th edition: https://cancerstaging.org/reference-s-tools/deskreferences/Documents/AJCC%20Breast%20Cancer%20Staging%20System.pdf
Cancer M stage: 0/1/X	As per AJCC 8 th edition
In view of the COVID-19 pandemic, was the management of this patient's breast cancer: Standard / Altered due to COVID-19	
Has the patient been tested for SARS-CoV2: Yes - tested positive Yes - tested negative Not tested Unknown Symptomatic, but not tested	
What was the diagnosis of COVID19 based on? SARS-CoV-2 antigen (RT-PCR) / CXR (e.g. consolidation) / CT (e.g. ground-glass)	
Date tested positive for SARS-CoV2.....dd/mm/yy	
If the first test was positive. Was a second test done? Yes/No	
If a second test done, what was the date?	
WHO performance status	0= able to carry out all normal activity without restriction 1= restricted in strenuous activity but ambulatory and able to carry out light work 2= ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours 3= symptomatic and in a chair or in bed for greater than 50% of the day but not bedridden

	4= completely disabled; cannot carry out any self-care; totally confined to bed or chair
Section 2: Category of 'altered management' as a result of COVID-19 (select all that apply) Completing this section will enable participating units to easily identify (using RedCap's built-in analysis tools) patients that fall within a defined category of COVID-altered treatment, for audit and service planning purposes.	
What was the COVID-ALTERED management plan (pre-operatively)?	
COVID-altered pre-operative imaging assessment (including biopsy): <ul style="list-style-type: none"> - No MRI performed for lobular cancer - amended imaging assessment of response to neo-adjuvant chemotherapy - Incidental/satellite ipsilateral lesion not assessed with biopsy - Altered assessment of B3 lesions - Other 	This includes patients who have had a diagnostic pathway that is outside of normal protocol.
Omitted neoadjuvant chemotherapy, when standard management would have included this	This includes patients who would usually have neoadjuvant chemotherapy as per local protocols, and those who would usually have 'down-staging' to accommodate BCS or TAD
Patient having 'incomplete' or 'nonstandard' neoadjuvant chemotherapy	A shortened or incomplete course of chemotherapy, <u>directly</u> due to COVID-19. This does <u>not</u> include patients who have had partial courses for side effects / complication only.
Patient with hormone receptor positive cancer having 'bridging' neoadjuvant endocrine therapy due to a potential delay in surgery	This includes patients in whom endocrine therapy had been used as a 'holding measure' <u>directly</u> due to the impact of COVID-19.
Patient given neo-adjuvant radiotherapy	
What was the ALTERED management plan (surgical)? THIS IS AT THE TIME OF CONSENT FOR SURGERY	This is the <u>planned</u> treatment at the time of consent for surgery
Patient expected to have / has had, a delay in surgery (>31 days from diagnosis)	
Patients having breast conserving surgery with NO/UNKNOWN planned radiotherapy (when standard management would have included adjuvant radiotherapy)	
Simple mastectomy in patients whose standard therapy would otherwise have been breast conservation followed by adjuvant radiotherapy	This is the patient whose choice for simple mastectomy over BCS was influenced by the unavailability of radiotherapy.

Simple mastectomy performed, with a view to delayed reconstruction, in patients who have been offered immediate reconstruction	This is the patient in whom a formal reconstruction discussion / assessment may not have been done, but patient was deemed likely to be appropriate (and has expressed in interest) for immediate recon in non-covid situation.
Patient with confirmed high risk, having mastectomy, who are not having synchronous contralateral risk-reducing mastectomy.	
Patient who would usually have margin re-excision surgery for close margins (based on local protocols), who do not have further surgery.	
Patient who would usually have completion axillary clearance for sentinel node macro-metastases, who do not have further surgery	
Patient who would usually have a sentinel node biopsy for incidental invasion found during surgery for DCIS, but has not had this.	
What was the ALTERED management plan (adjuvant)?	
Patient who would usually have adjuvant radiotherapy, but have not been offered this	
Patient having 'altered' radiotherapy, with 5 fractions	
Patient who would usually have adjuvant chemotherapy, but have not been offered this	
Patient who would usually have adjuvant targeted (e.g. herceptin) therapy, but have not been offered this	
Genomic testing (e.g. ONCOTYPE) used outside of NICE guidelines (2018) to direct adjuvant chemotherapy	
Section 3: Amended management plan (in view of the COVID-19 pandemic) NOTE: This section will only appear if you have selected 'COVID-altered treatment' in section 1 above. The 'Pre-COVID' data field refers to the standard planned treatment, that the patients would have undergone in normal circumstances, prior to the COVID-19 pandemic. The 'COVID' data field refers to the revised planned treatment in view of the COVID-19 pandemic.	
<u>Pre-operative treatment (Pre-COVID and COVID-ALTERED):</u> None, surgery first / neoadjuvant chemotherapy / neoadjuvant endocrine therapy / primary endocrine therapy / neoadjuvant radiotherapy	
<u>Surgical treatment – Breast (Pre-COVID and COVID ALTERED):</u> BCS / simple mastectomy / skin sparing or nipple sparing mastectomy and immediate reconstruction / consideration of BCS following neoadjuvant chemotherapy	

<u>Surgical treatment - Axilla (Pre-COVID and COVID ALTERED):</u> No axillary surgery / sentinel node biopsy / axillary clearance / consideration of axillary preservation following neoadjuvant chemotherapy	
<u>Adjuvant Chemotherapy (Pre-COVID and COVID ALTERED):</u> no / yes	
<u>Adjuvant Targeted therapy (Pre-COVID and COVID ALTERED):</u> no/yes If yes; Trastuzumab only/ Pertuzumab only / Combination therapy	
<u>Adjuvant Radiotherapy (Pre-COVID and COVID ALTERED):</u> no / yes / yes, but hypofractionated / yes, but boost not given	
<u>Adjuvant Endocrine therapy (Pre-COVID and COVID ALTERED):</u> no / yes	
Section 4. Further (anonymised) patient demographic and cancer information This section is optional during the prospective data collection.	
Menopausal status: Size of lesion on pathology & imaging / Menopausal status / ER / PR / HER2 / KI67 / lymph node macro-metastases / lymph node micro-metastases / Co-morbidities	If bilateral or multifocal cancer, please enter data for the cancer for which an 'altered' pathway of management was recommended (bilateral), or the largest lesion (multifocal).
Section 5. Outcome data	
This section will be finalised following consultation with sub-groups of the steering management group, and will be driven by the volume of patients that fall within the defined categories of COVID-altered treatment.	
THE FOLLOWING QUESTIONS RELATE TO PATIENTS ON NEOADJUVANT 'BRIDGING' ENDOCRINE THERAPY (NET).	
PLEASE ENSURE THAT THE PRE-OPERATIVE DATA IS COMPLETED IN SECTION 4.	
IF THERE ARE NO QUESTIONS DISPLAYED, THEN THIS CATEGORY DOES NOT APPLY TO THIS PARTICULAR PATIENT.	
Date started on NET? (dd-mm-yy)	
What hormone therapy was prescribed? Anastrozole / Letrozole / Exemestane / Tamoxifen / Zoladex	
Pre-operative Lymph node status Normal lymph nodes on USS or reactive nodes on biopsy / Abnormal lymph nodes on USS, core biopsy shows metastatic disease / Abnormal lymph nodes on USS, FNA shows metastatic disease	

Was a clip placed in the lesion? No / Yes, using USS guidance / Yes, using stereo guidance / Yes, using MRI guidance	
Length of time on NET (in days)	This will be automatically calculated using the date started NET above and date of surgery in section 1.
Was follow-up imaging performed prior to surgery (following a period of NET)? No / Yes, USS / Yes, MMG / Yes, MRI	
Size of lesion on follow-up MMG / USS / MRI (largest dimension, in mm)	This is the largest dimension as recorded on the imaging report.
Was Ki67 repeated on a second core biopsy or the surgical excision specimen? Yes/No	
If so, value?	
What was the rationale for choosing the date of surgery? This was the planned date, for when sufficient theatre capacity was available / Surgery expedited due to early availability of theatre capacity / Surgery expedited due to lack response / Surgery expedited due to intolerance of NET or compliance	
In patients with a pre-NET plan for mastectomy, was adequate down staging achieved to accommodate for breast conservation instead? No, patient proceeded with planned mastectomy Yes, patient had breast conserving surgery Yes, but patient elected to have mastectomy	Note: Therapeutic mammoplasty would be considered breast conserving surgery, and details of this are not specifically collected.
THE FOLLOWING QUESTIONS RELATE TO PATIENTS WHO ARE COVID+ve	
PLEASE ENSURE THAT THE PRE-OPERATIVE DATA IS COMPLETED IN SECTION 4.	
IF THERE ARE NO QUESTIONS DISPLAYED, THEN THIS CATEGORY DOES NOT APPLY TO THIS PARTICULAR PATIENT.	
What was the patient's BMI?	
What was the impact of the patient's COVID19 infection on their management pathway? No impact / Delay in Surgery, but surgery still primary treatment / Conversion to neoadjuvant chemotherapy, and delayed surgery / Conversion to 'bridging' neoadjuvant endocrine therapy, and delayed surgery / Admission to hospital resulting in delay in breast surgery (>31 days) due to discharge to rehab etc.	
Was the patient admitted to the hospital following a diagnosis of COVID-19? No - managed at home / Yes – Ward / Yes – HDU / Yes - ICU	

<p>If HDU/ICU support required, what respiratory support was needed? Advanced respiratory support (IMV, ECMO) / Basic respiratory support (NIV / CPAP, high flow O2) / Cardiovascular support (inotropes, etc) / Renal support – CVVHD / Proning</p>	
<p>Were any COVID19 specific medical treatments employed? Azithromycin / Hydroxychloroquine / Macrolides / Steroids / Interferon-beta-1a / Tocilizumab (anti-IL-6R) / Anakinra (Anti-IL-1Ra) / Sarilumab (anti-IL-6R) / Lopinavir-Ritonavir / Oseltamivir / Convalescent plasma / Remdesvir</p>	

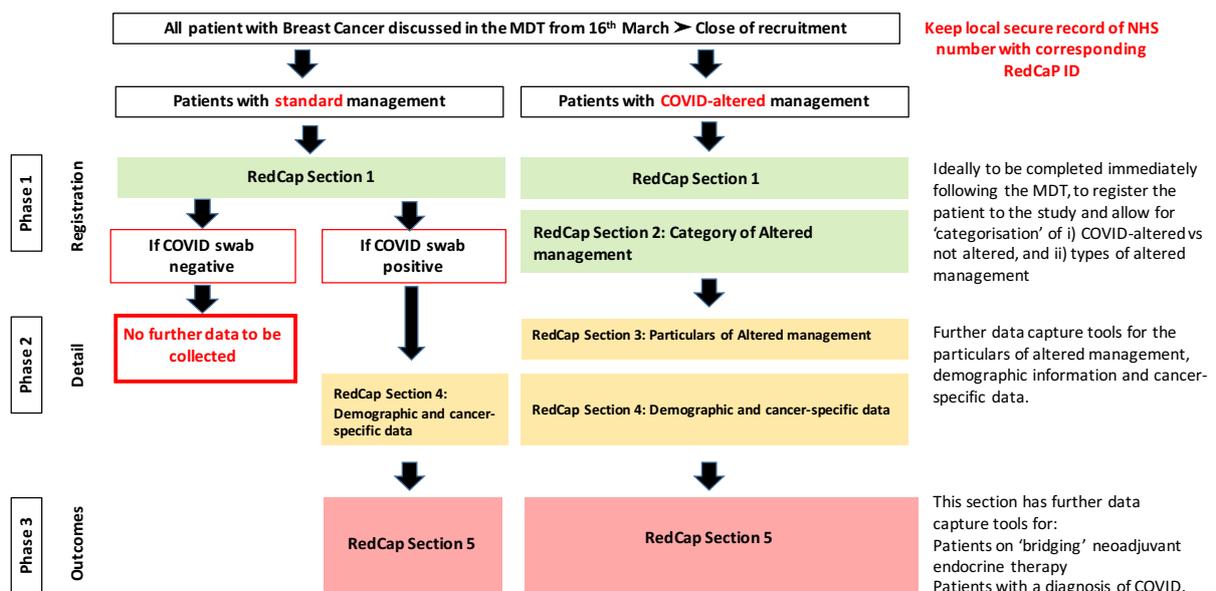
4.3 Data capture phases

It is likely that the data capture will occur in several phases.

Phase 1 – This will ideally be prospective where possible. This will ‘register’ the patient to the study and classify the patient’s management to the appropriate COVID-altered category as per section 2 on RedCap.

Phase 2 – This can be collected prospectively or retrospectively where possible. Section 3 and 4 on RedCap include data capture tools for the exact particulars of COVID-altered management, demographic information and cancer-specific data.

Phase 3 – Outcome data will be finalised following completion of phase 1, and will occur following consultation with sub-groups of the steering management group.



Post COVID-19 questionnaire

The audit will close to recruitment once breast cancer services have returned to normality and breast cancer management decisions are no longer being altered in view of COVID-19.

A questionnaire will be sent out, as designed by the audit steering committee and advisory group. This will include, but will not be limited to:

- The number of patients being treated in the unit over the study period
- The variations in the logistics of delivery of surgical care
- The impact on the service in the post-COVID era

5. Data management and storage

Data collection will occur in accordance with Caldicott II principles. Data for each patient will be pseudo-anonymised using a unique alphanumeric study identification number. No patient identifiable data will be recorded for the purpose of the audit.

Study data will be collected and managed using REDCap electronic data capture tools hosted at University of Manchester and made freely available to research collaboratives in the UK (21). REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. More information about the consortium and system security can be found at <http://www.projectredcap.org/>.

6. Data analysis

All data analysis will occur centrally and will be led by the steering group. All individual units will have access to download their own data and perform their own analyses. Local collaboratives and hospital Trusts will have ownership of their own data and will be able to present it locally if they so wish.

Simple summary statistics will be calculated for each outcome and regression analysis used to control for predictive variables. Data will be tested for distribution and differences

between groups using unpaired t-tests, Mann-Whitney U tests and Chi squared tests as appropriate. There is no power calculation for this audit.

7. Publication and authorship policy

All presentations and publications will be made on behalf of the B-MaP-C Research Collaborative.

Three levels of authorship are proposed based on degree of study participation:

7.1 Named authors

Named authors will be required to meet the International Committee of Medical Journal Editors (ICMJE) criteria (www.icmje.org) for authorship based on the following four criteria:

1. Substantial contribution to the conception or design of the work; or the acquisition, analysis or interpretation of the data for the work and
2. Drafting the work or revising it critically for important intellectual content and
3. Final approval of the version to be published and
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

The ICMJE states 'when submitting a manuscript authored by a group, the corresponding author should specify the group name if one exists and clearly identify the group members who can take credit and responsibility for the work as authors. The byline of the article identifies who is directly responsible for the manuscript and MEDLINE lists authors whichever names appear on the byline. If the byline includes a group name, MEDLINE will list the names of individual group members who are authors or who are collaborators, sometimes called non-author contributors, if there is a note associated with the byline clearly stating that the individual names are elsewhere in the paper and whether those names are authors or collaborators.'

It is anticipated that between six and eight individuals will be named on each publication followed by the wording 'on behalf of the B-MaP-C Research Collaborative'. All citable collaborators will be listed at the end of the paper and their roles identified.

7.2 Citable collaborators

Citable collaborators will have made a considerable contribution to the study, but will not have met the ICMJE criteria for authorship (non-author contributors). These will include trainee or consultant leads at each centre and other trainees or team members (including consultant surgeons, clinical nurse specialists or research nurses) who have recruited at least 10 complete case records to the study.

7.3 Acknowledged collaborators

Acknowledged collaborators will include consultant surgeons who contributed patients to the audit, but did not personally collect data or recruit patients and trainees who have made a lesser contribution to patient recruitment and data collection than that required for citable collaborator status. Trainees who are acknowledged contributors will also receive a certificate of participation for inclusion in their portfolios.

The final reports will be prepared in accordance with the STROBE(24) (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

8. Audit Governance

The main aim of the audit is to document and describe breast cancer management (surgery, neoadjuvant/adjuvant chemotherapy and radiotherapy) during the COVID-19 pandemic.

A unit lead will be identified, who will coordinate the audit locally, in keeping with local protocol and policies. It is assumed that all breast cancer patients will be discussed at MDT, and their standard/COVID-altered treatment pathways clearly recorded in the usual fashion. Patients undergoing COVID-altered management pathways will be identified at the MDT discussion and reported to the unit project lead. Attendance at MDT by the unit project lead will be at the discretion of local protocols and policies.

The named unit project lead will act as the principal investigator for each unit (likely a nominated consultant). Audit approval will need to be sought from the Clinical Audit Department for the project prior to commencing data collection, and the audit reference number emailed to COVID19breast@gmail.com.

See appendix 1 for frequently-asked questions for completion of audit approval.

Each unit participating in B-MAP-C will retain full ownership of its own data. Authorship on publications will follow the guidance in section 7, above. Summary statistics will be calculated for each participating region and fed back to individual units to allow comparison with national averages and ranges. Overall audit results and results from individual centres will be fed back to the Association of Breast Surgery.

9. Audit Management

The Audit Steering Committee (ASC) will

- i) maintain oversight of the B-MAP-19 national audit. This will include management and data ownership of global data entered onto RedCap.
- ii) assess future applications for access to the global B-MAP-C dataset with regards to putative research or audit projects. The committee will be advised on these applications by the Audit Advisory Group.
- iii) lead future applications to grant awarding bodies in order to conduct ethically approved research / outcomes studies using the B-MAP-C dataset.
- iv) work with the audit advisory group to respond to any potential future challenges to the audit

The Audit Advisory Group will

- i) advise the ASC on the running of the B-MAP-C national audit
- ii) liaise with other national bodies (eg Association of Breast Surgery) or national audits (eg Cancer Outcomes Services Dataset, National Audit on Breast Cancer in Older Patients) such that added value is brought to the B-MAP-C audit.
- iii) advise the ASC on the merits of applications for access to national B-MAP-C dataset
- iv) following discussion with the ASC, lead or initiate future audit projects using the B-MAP-C dataset
- v) following discussing with the ASC, lead or initiate future grant applications to in order to conduct ethically approved research / outcomes studies using the B-MAP-C dataset
- vi) work with the ASC to respond to any potential future challenges to the audit

10. References

Reference List

1. Velavan TP, Meyer CG. The COVID-19 epidemic. *Trop Med Int Health*. 2020;25(3):278-80.
2. Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. 2020.
3. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020.
4. <https://associationofbreastsurgery.org.uk/media/252009/abs-statement-150320-v2.pdf> [
5. <https://associationofbreastsurgery.org.uk/media/252006/nccbp-abp-covid-19-breast-pathology-guidance.pdf>]
6. Coles CE, Aristei C, Bliss J, Boersma L, Brunt AM, Chatterjee S, et al. International Guidelines on Radiation Therapy for Breast Cancer During the COVID-19 Pandemic. *Clin Oncol (R Coll Radiol)*. 2020;32(5):279-81.
7. <https://www.rcr.ac.uk/sites/default/files/breast-cancer-treatment-covid19.pdf> [
8. <https://www.rcr.ac.uk/sites/default/files/pre-operative-breast-radiotherapy-covid-19.pdf> [
9. van de Haar J, Hoes LR, Coles CE, Seamon K, Fröhling S, Jäger D, et al. Caring for patients with cancer in the COVID-19 era. *Nature Medicine*. 2020.
10. Bhangu A, Koliias AG, Pinkney T, Hall NJ, Fitzgerald JE. Surgical research collaboratives in the UK. *Lancet (London, England)*. 2013;382(9898):1091-2.
11. Koliias AG, Cowie CJ, Tarnaris A, Hutchinson PJ, Brennan PM. Ensuring a bright future for clinical research in surgery with trainee led research networks. *BMJ (Clinical research ed)*. 2013;347:f5225.
12. Koliias AG, Jones TL, Cowie CJ, Coulter IC, Afshari FT, Tarnaris A, et al. A report from the inaugural meeting of the British Neurosurgical Trainee Research Collaborative held in the Royal College of Surgeons of England, 19 October 2012. *British journal of neurosurgery*. 2013;27(3):307-10.
13. Pinkney TD, Calvert M, Bartlett DC, Gheorghie A, Redman V, Dowswell G, et al. Impact of wound edge protection devices on surgical site infection after laparotomy: multicentre randomised controlled trial (ROSSINI Trial). *BMJ (Clinical research ed)*. 2013;347:f4305.
14. Ferguson HJ, Hall NJ, Bhangu A. A multicentre cohort study assessing day of week effect and outcome from emergency appendicectomy. *BMJ quality & safety*. 2014;23(9):732-40.
15. Multicentre observational study of performance variation in provision and outcome of emergency appendicectomy. *The British journal of surgery*. 2013;100(9):1240-52.
16. Potter S, Conroy EJ, Cutress RI, Williamson PR, Whisker L, Thrush S, et al. Short-term safety outcomes of mastectomy and immediate implant-based breast reconstruction with and without mesh (iBRA): a multicentre, prospective cohort study. *Lancet Oncol*. 2019;20(2):254-66.
17. O'Connell RL, Rattay T, Dave RV, Trickey A, Skillman J, Barnes NLP, et al. The impact of immediate breast reconstruction on the time to delivery of adjuvant therapy: the iBRA-2 study. *Br J Cancer*. 2019;120(9):883-95.
18. O'Connell RL, Baker E, Trickey A, Rattay T, Whisker L, Macmillan RD, et al. Current practice and short-term outcomes of therapeutic mammoplasty in the international TeaM multicentre prospective cohort study. *The British journal of surgery*. 2018;105(13):1778-92.
19. Dodwell D, Clements K, Lawrence G, Kearins O, Thomson CS, Dewar J, et al. Radiotherapy following breast-conserving surgery for screen-detected ductal carcinoma in situ: indications and utilisation in the UK. Interim findings from the Sloane Project. *Br J Cancer*. 2007;97(6):725-9.
20. Jauhari Y, Gannon MR, Dodwell D, Horgan K, Tsang C, Clements K, et al. Addressing frailty in patients with breast cancer: A review of the literature. *Eur J Surg Oncol*. 2020;46(1):24-32.

21. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*. 2009;42(2):377-81.
22. Obeid JS, McGraw CA, Minor BL, Conde JG, Pawluk R, Lin M, et al. Procurement of shared data instruments for Research Electronic Data Capture (REDCap). *Journal of Biomedical Informatics*. 2013;46(2):259-65.
23. Boland MR, Rusanov A, So Y, Lopez-Jimenez C, Busacca L, Steinman RC, et al. From expert-derived user needs to user-perceived ease of use and usefulness: A two-phase mixed-methods evaluation framework. *Journal of Biomedical Informatics*. in press.
24. Elm Ev, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ (Clinical research ed)*. 2007;335(7624):806-8.

Appendix 1: Frequently asked questions for Audit registration

What is the rationale for undertaking this audit?

The COVID-19 pandemic has led to worldwide repercussions in healthcare delivery, including that of cancer care. Management of patients confirmed to have breast cancer may involve an 'altered' treatment pathway. It is clear that there is much to learn from this, particularly with the anticipated de-escalation of adjuvant treatment and potential delay in surgery.

What is the principle aim of the audit?

To document and describe breast cancer management (surgery, neoadjuvant / adjuvant chemotherapy and radiotherapy) during the COVID-19 pandemic and compare this to current accepted (pre-COVID-19) practice.

What are the standards being measured by this clinical audit?

The aim of this audit is to document and describe the management of breast cancer that is 'altered' in view of the COVID-19 pandemic. This will be compared against standard accepted and published breast cancer management pathways and outcomes.

What is the source of standards?

Standard accepted and evidence-based breast cancer management pathways, as recommended by NICE, The Association of Breast Surgeons, and the published literature.

How do you intend to collect data?

Identification of patients with 'altered' management (in view of COVID-19) will occur at the MDT meeting. Further non-identifiable data will be collected from the patient records. Data collection will occur in accordance with Caldicott II principles. Study data will be collected and managed using REDCap electronic data capture tools hosted at University of Manchester. Data for each patient will be pseudo-anonymised using a unique alphanumeric study identification number. A local secure record of the NHS number corresponding to the study identification number will be kept, but not uploaded - NO patient identifiable data will be uploaded for the purpose of the audit

What do you expect the sample size to be?

(The number of patients expected to be treated for cancer over a 3-month period).

How will this data be analysed and disseminated?

All data analysis will occur centrally and will be led by the steering group. The breast unit will have ownership of our own local data, which we are able to present locally and to use for capacity planning in the post-COVID phase.